

**Remarks**

No claims have been cancelled or added, and claims 2, 6, 7 and 9 have been amended. Accordingly, claims 1-13 are still pending in the current application. The amendments to claims 2 and 6 are fully supported by the specification and do not introduce new matter. Claims 2, 6, 7 and 9 were amended to correct typographical errors, and claim 6 was also amended to more accurately capture the commercial embodiments covered by the pending claims. Applicants have taken the opportunity in this response to the Notice of Non-Compliant Amendment to further amend claims 2, 6, 7 and 9, solely to correct typographical errors that were not corrected in the July 21, 2004 submission. Applicants are not surrendering any equivalents by way of these amendments.

**Objections by Examiner: Informalities**

The Examiner objects to Claim 2 for being depend upon itself. Applicants thank the Examiner for pointing out this typographical error. Claim 2 has been amended to remove the objection.

**The Examiner's Rejection under 35 U.S.C. §112, first paragraph is Traversed**

The Examiner has rejected Claims 1-13 under 35 U.S.C. §112 First Paragraph, stating:

“ . . . others skilled in the art would be unable to practice the invention as claimed without undue experimentation and with a reasonable expectation of success, other than using a mutated glucose binding protein which includes one amino acid substitution selected from the group consisting of a cysteine at position 74, a cysteine at position 149, or a cysteine at position 213 results [*sic*] in signal-enhanced glucose detection as evidenced by figure 1 and figure 8 of the instant application.”

(Office Action, March 22, 2004, page 4)

In making the rejection, the Examiner focuses on the mutant protein of claims 1-13 and asserts that “the claims broadly encompass a group of amino acid substitutions for a mutated glucose binding protein which are clearly beyond the scope of the instant disclosure.” (Office Action, March 22, 2004, page 3). Applicants respectfully disagree with the Examiner’s assessment of the specification in relation to mutated binding proteins.

The Examiner acknowledges that the specification is enabling for a mutated binding protein with amino acid substitutions cysteine at positions 74, 149 and 213. Thus, the Examiner acknowledges that representative examples of the claimed genus of mutant binding proteins are enabled. Additionally, Examples of mutated protein synthesis are given in paragraphs [0052]-[0059] of Applicants' specification. The Examiner is reminded that

[f]or a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus *only where adequate reasons are advanced by the examiner* to establish that a person skilled in the art could not use the genus as a whole without undue experimentation.

Manual of Patenting Examination Procedure, 8<sup>th</sup> Ed. §2164.02 (emphasis added).

The above passage indicates that the level of skill in the art and the state of the art must be taken into account when determining if a specification is enabling. These two factors are also listed in *In re Wands*, as well as in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). Both the level of skill in the art and the state of the art are such that preparing mutant proteins is *not* a matter of undue experimentation. And, as the Federal Circuit espoused in *In re Wands*, “[e]nabling is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. ‘The key word is ‘undue,’ not ‘experimentation.’” *In re Wands* 858 F.2d 731,736-737 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d at 504). Upon request, Applicants will gladly provide the Examiner with references demonstrating that mutant protein engineering was a part of the state of the art at the time of filing.

In view of the admission by the Examiner that representative examples of the claimed genus are enabled, and in view of the state of the art at the time filing, the Examiner must therefore advance adequate reasons why one of skill in the art would not be able to practice the entire scope of the claimed invention. To that end, the Examiner is invited to file a Declaration

Under 37 C.F.R. § 1.104(d)(2) outlining the facts behind the position that the specification does not fully enable the scope of the claimed invention.

Applicants assert that the specification is fully enabled for the entire breadth of the claimed invention. Reconsideration and withdrawal of the outstanding enablement rejection is earnestly solicited.

**The Examiner's Rejection under 35 U.S.C. §102(b) is Traversed**

The Examiner has rejected claims 1-13 under 35 U.S.C. 102(b) as being anticipated by Lakowicz (US 6197534) or by Hellingsa (US 6277627). The Examiner states:

The instant invention is drawn to a biosensor comprising at least one mutated binding protein and at least one thiol group *and at least one sensor surface* which provides a detectable signal resulting from a change in refractive index when the mutated binding protein binds to analyte. Each of the cited references teach a sensor comprising a modified glucose binding protein. (see '534 patent 30, 32, 33, 34, 35, 37, 38. and 40, columns 15 and 16 and '627 patent, claim 1, column 11). Further, Lakowicz [sic] et al. expressly teach the protein is modified by substituting at least one cysteine residue (see claims 37 and 38, columns 15 and 16). Accordingly, each of the cited references is deemed to anticipate the above claims. [emphasis added]

Applicants respectfully traverse the rejection.

To anticipate, a prior art reference must teach each and every element of the claim. As stated by the Examiner, Applicants instant claims recite a biosensor comprising at least one mutated binding protein and at least one thiol group *and at least one sensor surface*. Neither Lakowicz or Hellingsa teach or suggest even suggest, among other things, the combination of a mutant protein and sensor surface, as claims 1-13 require. Accordingly, neither Lakowicz nor Hellingsa anticipates the claimed invention. Reconsideration and withdrawal of the rejection is respectfully requested.

**The Examiner's Rejection under 35 U.S.C. §103 is Traversed**

The Examiner has rejected claims 1-13 under 35 U.S.C. 103(a) as being obvious over Lakowicz et al., (US 6,197,534) or Hellingsa (US 6,277,627). The Examiner states:

The references are relied upon for the reasons set forth above. The adjustment of particular conventional working conditions (e.g., at least one thiol group attached to at least one mutated binding protein) is deemed clearly to be a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan, based upon the beneficial [*sic*] teachings provided by one or more of the cited references with respect to a biosensor comprising at least one mutated binding protein selected from glucose binding protein.

Applicants respectfully traverse the rejection.

To establish a case of *prima facie* obviousness, the Examiner must meet three criteria. First, the Examiner must show that the references upon which she or he relied teach *every* limitation of the currently claimed invention, *In re Royka* 490 F.2d 981, 985 (C.C.P.A. 1974). Second, the Examiner must show that there is some suggestion or motivation in the references themselves, or within the knowledge of one of ordinary skill in the art, to alter or combine references to arrive at the claimed invention. Lastly, the Examiner must show that there is a reasonable expectation of success in altering or combining the references, and that this expectation of success is found in the references as well. *In re Vaeck* 947 F.2d 488, 493 (Fed. Cir. 1991). Applicants assert that the Examiner has not met any of these criteria and thus can not sustain an assertion that the claims are obvious to one of ordinary skill in the art.

As stated previously, neither Lakowicz nor Hellinga teach the combination of a mutant protein with a surface sensor. In addition, both Lakowicz and Hellinga fail to teach detection of analyte binding by measuring changes in refractive index. Instead, Lakowicz and Hellinga each teach detection of analyte binding by measuring changes in fluorescence. There is no motivation to alter either Lakowicz or Hellinga to include a surface sensor, and there is no motivation to change the method of detection. Indeed, the Examiner can not provide any suggestion or alter the teachings of Lakowicz or Hellinga to arrive at the claimed invention, because no such motivation exists. Thus, because the Examiner has failed to meet all three criteria necessary to establish a *prima facie* case of obviousness, Applicants assert that the Examiner does not and can not sustain his burden in establishing a *prima facie* case of obviousness. Reconsideration and withdrawal of the rejection is respectfully requested.

**Conclusion**

Applicants have amended claims 2 and 6, and claims 1-13 are still pending in the current application. The amendments to claims 2 and 6 are fully supported by the claims and do not constitute new matter.

Claim 2 has been amended to remove the Examiner's objection. Additionally, Applicants have addressed and traversed all of the stated grounds for rejection each of the Examiner's rejection posed in the April 22, 2004 Office Action. Applicants therefore respectfully assert that the present application is in condition for allowance. Early notification to this effect is earnestly solicited.

It is not believed that any fees are required, beyond those provided in the July 21, 2004 response to Office Action. If, however, additional extensions of time are necessary to prevent abandonment of this application, then extensions of time are hereby petitioned under 37 C.F.R. §1.136(a), and any fees required, including fees for net addition of claims, are hereby authorized to be charged to account number 50-3120.

Should the Examiner believe that further discussion of any remaining issues would advance the prosecution, he or she is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

Date August 18, 2004

By Todd B. Buck

Castellano Malm Ferrario & Buck PLLC  
Customer Number: 43446  
Telephone: (202) 478-5300  
Facsimile: (202) 318-1288

Todd B. Buck  
Registration No. 48,574